

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: Farzan Rastinejad et al. :

APPLICATION NO.: 09/443,542 : Examiner: Gregory W. Mitchell

FILING DATE: November 19, 1999 : Group Art Unit: 1617

TITLE: METHODS AND COMPOSITIONS FOR :
RESTORING CONFORMATIONAL
STABILITY OF A PROTEIN OF THE p53
FAMILY

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Inventor Declaration under 37 CFR 1.132

I, Dr. Farzan Rastinejad, an inventor on the above-identified application, make this declaration in support thereof.

I received my Ph.D. degree from Northwestern University, Chicago, Illinois, in 1988. For the last eleven (11) years, I have been employed by Pfizer, Inc. where I am Senior Principal Investigator for Oncology.

The attached data printout sheets show the results of testing (according to the general protocol of Example 1 of the present application) of compounds to determine their efficacy in stabilizing the native conformation of p53. In Panel I of the printout (Pages 1-9), the "SC50" value ("stabilizing concentration") represents the concentration of the test compound (usually micromolar, unless the compound is reported as inactive or weekly inactive) needed to retain (per the Example 1 protocol) 50% of maximal binding of a p53-specific antibody whose binding to p53 is conformationally dependent (for non denatured p53). The periods of incubation vary somewhat, since the data was intended to be qualitative, useful for a broad comparison, but are generally about 30 minutes at about 37 degrees C.

The data evidence a wide variety of chemical compounds that bind to p53 and can stabilize it, including many as disclosed in the above-identified patent application. The data panels show a complete listing of all compounds tested in the panel, including large numbers of compounds that are not effective in the practice of the invention. Similarly, Panel 2 of the printout (the subsequently following Pages 1-33) shows additional compounds having activity according to the practice of the invention (again as measured by SC50, data in far right column), and the inactive compounds of this subsequent panel are also shown. The lack of a number in the far right hand column means that the compound was inactive.

I acknowledge that all statements made of my own knowledge, are true and that all statements made on information and belief are believed to be true.

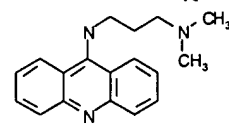
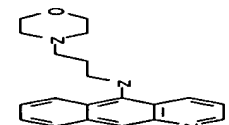
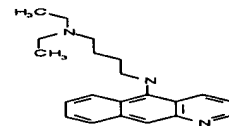
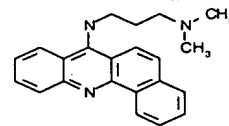
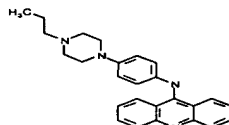
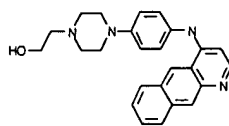
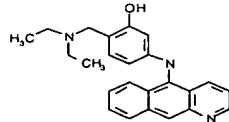
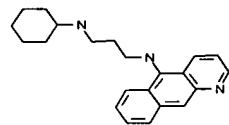
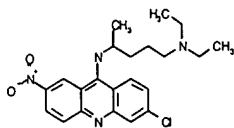
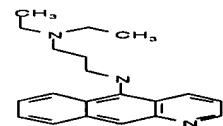
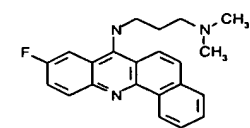
I further acknowledge that willful false statements, and the like, are punishable by fine or imprisonment, or both (18 USC section 1001) and may jeopardize the validity of the application or any patents issuing thereon.

Dated: _____

Dr. Farzan Rastinejad

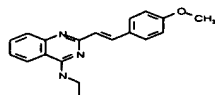
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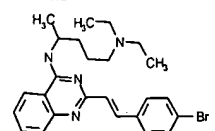


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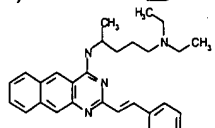
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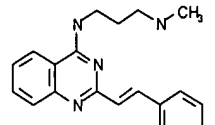
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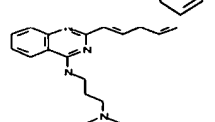
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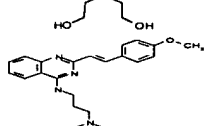
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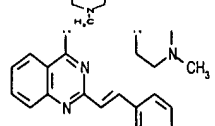
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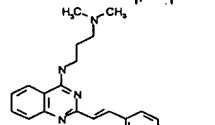
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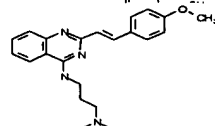
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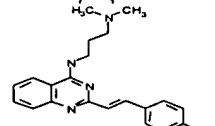
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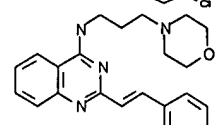
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SC50 (uM)

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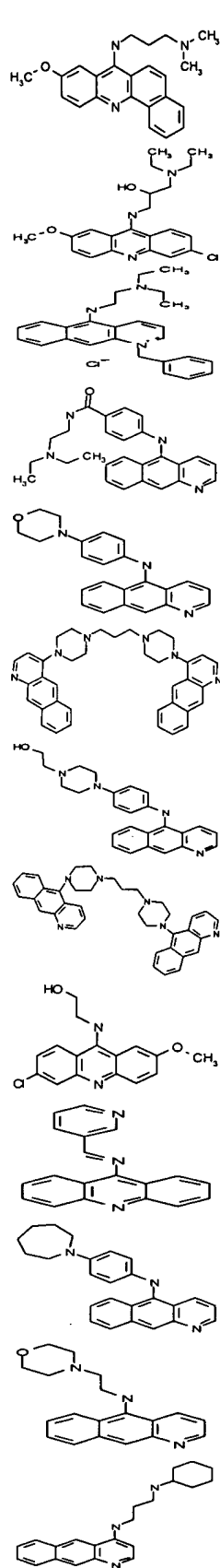
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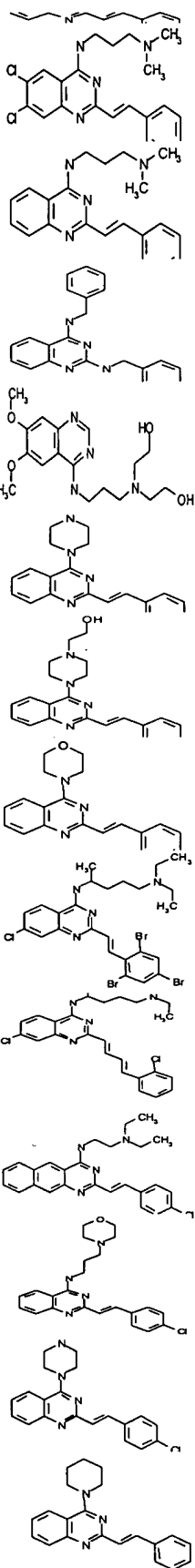
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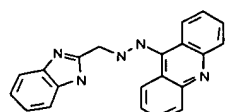
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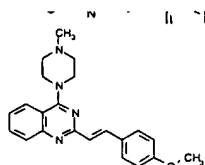
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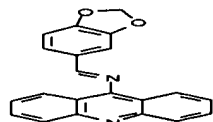
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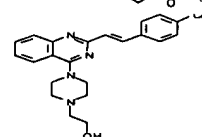
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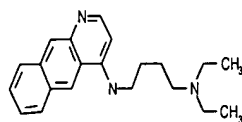
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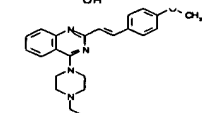
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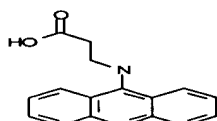
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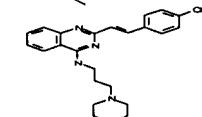
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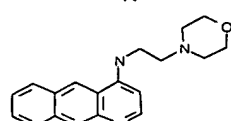
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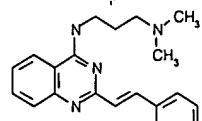
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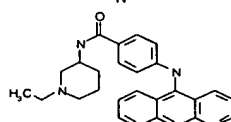
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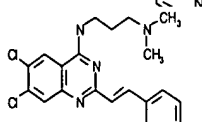
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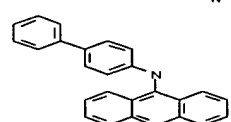
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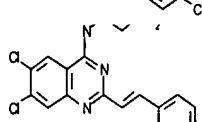
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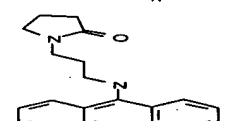
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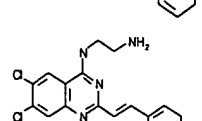
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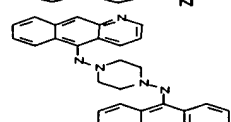
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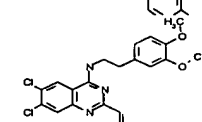
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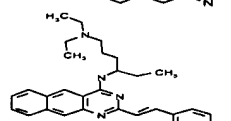
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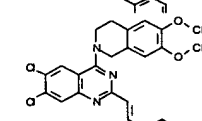
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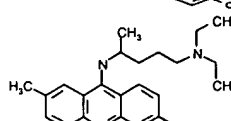
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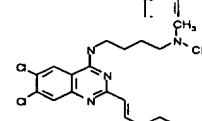
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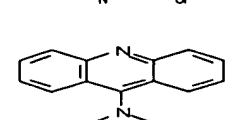
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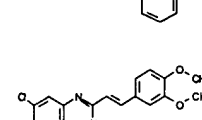
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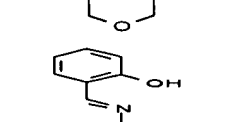
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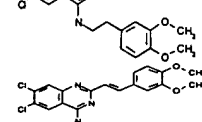
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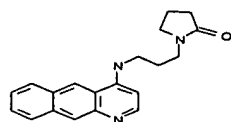


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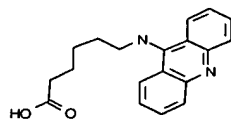
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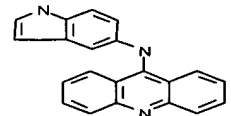
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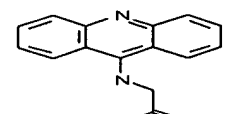
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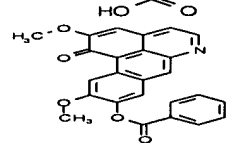
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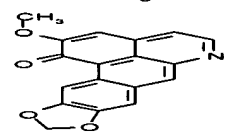
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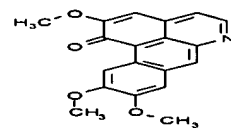
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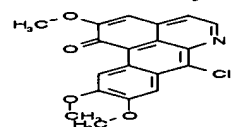
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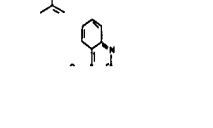
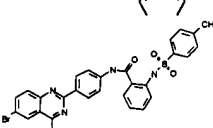
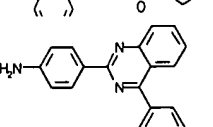
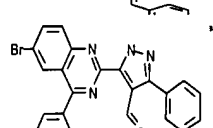
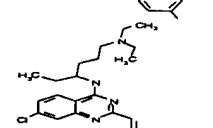
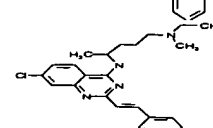
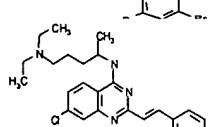
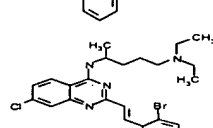
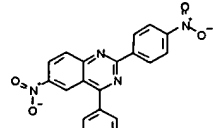
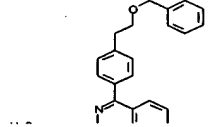
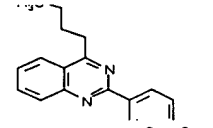
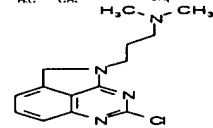
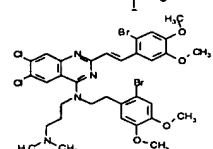
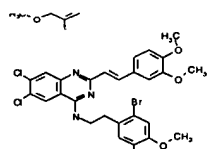
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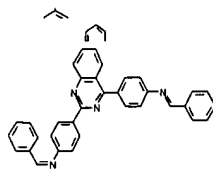


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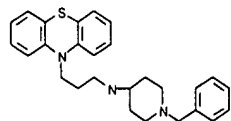


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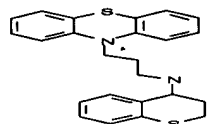
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SC50 (uM) MOLSTRUCTURE

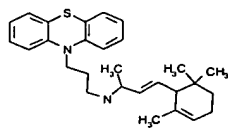
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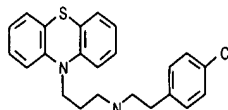
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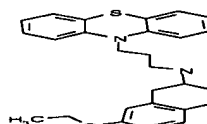
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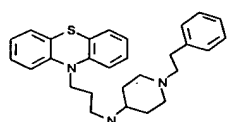
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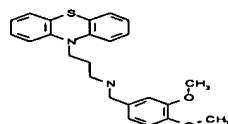
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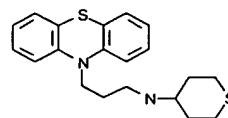
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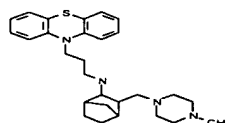
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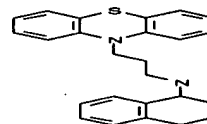
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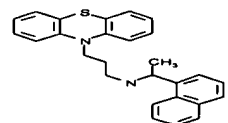
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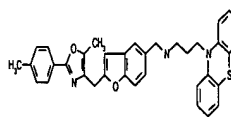
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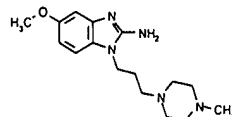
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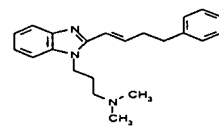
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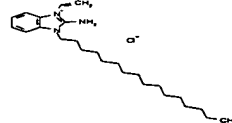
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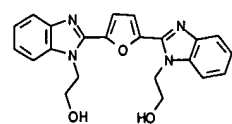
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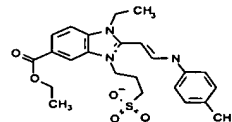
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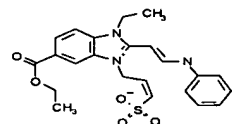
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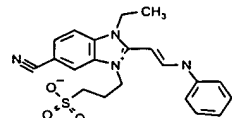
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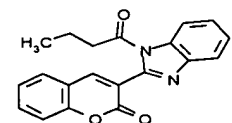
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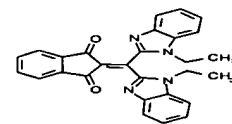
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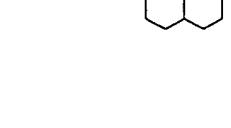
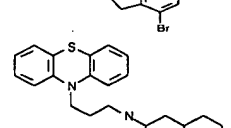
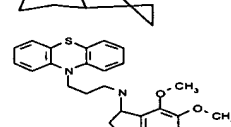
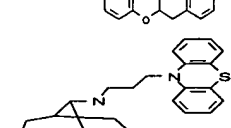
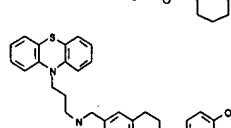
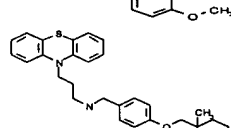
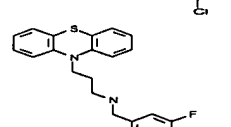
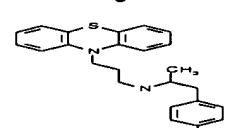
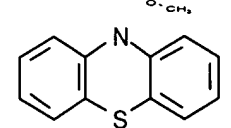
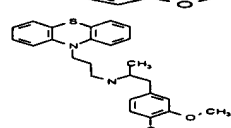
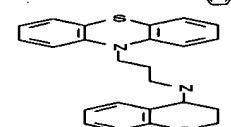
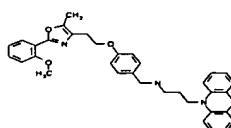
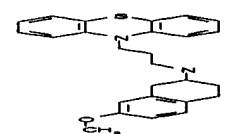
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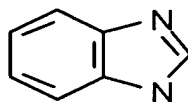
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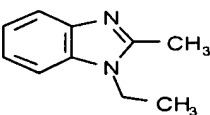


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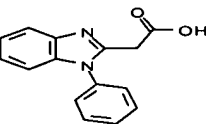
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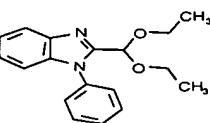
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42



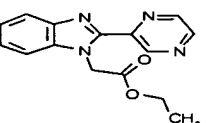
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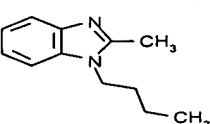
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67



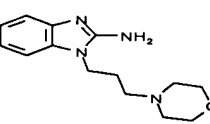
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INACTIVE



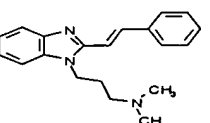
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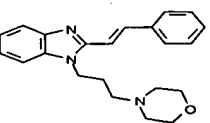
WEAK

WEAK



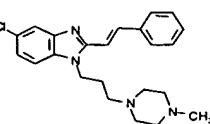
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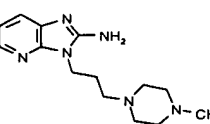
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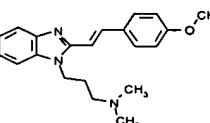
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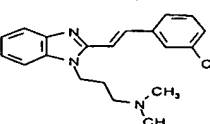
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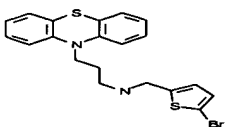
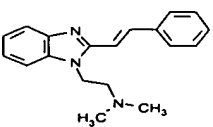
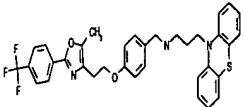
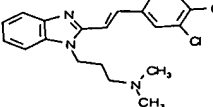
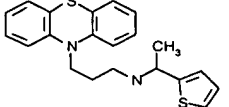
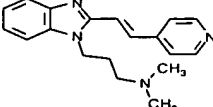
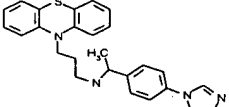
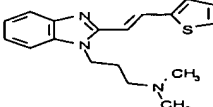
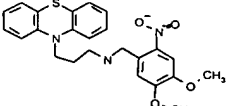
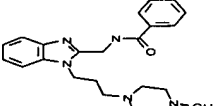
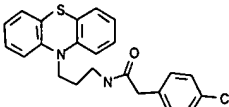
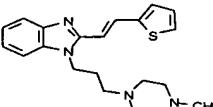
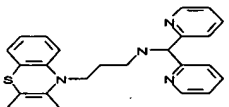
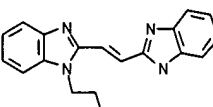
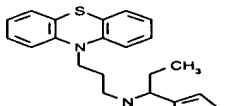
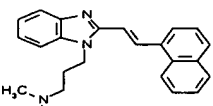
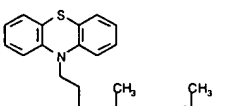
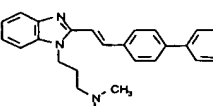
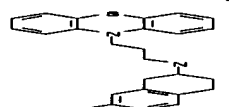
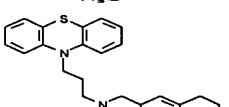
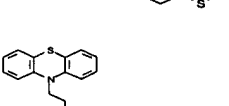
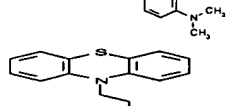
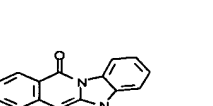


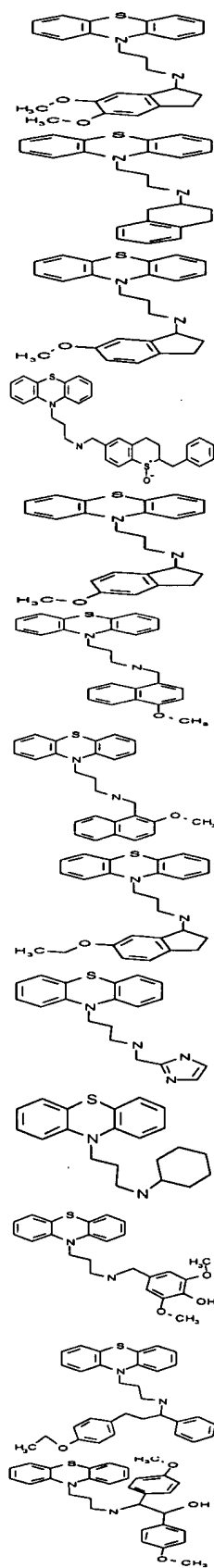
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WEAK-IN.

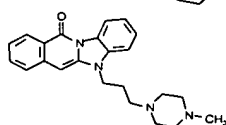


INACTIVE

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	INACTIVE		WEAK
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	INACTIVE		INACTIVE
	INACTIVE		INACTIVE
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	WEAK		INACTIVE

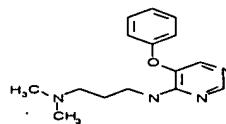


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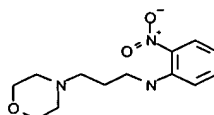
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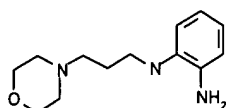
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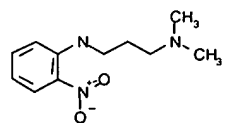
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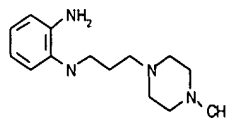
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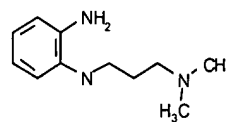
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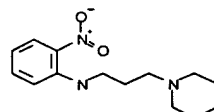
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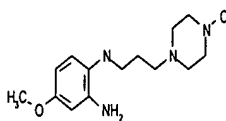
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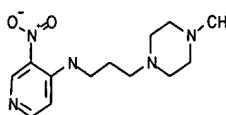
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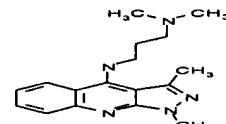
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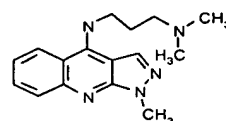
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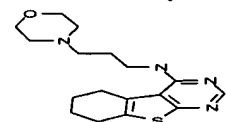
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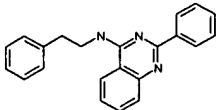
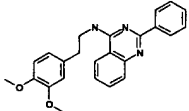
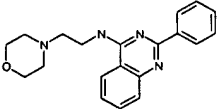
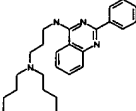
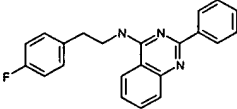
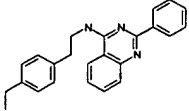
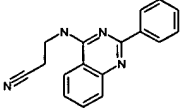
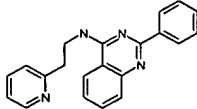
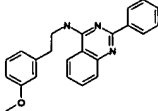
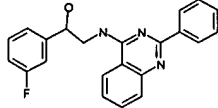
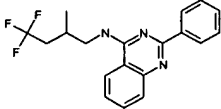
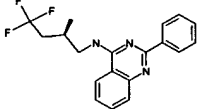
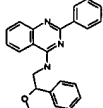


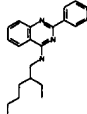
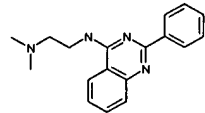
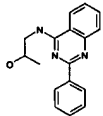
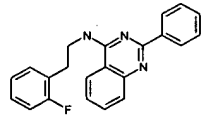
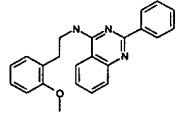
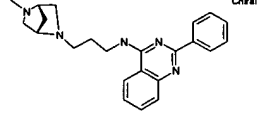
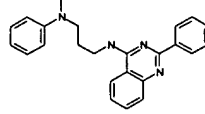
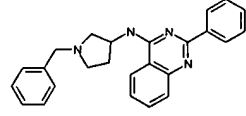
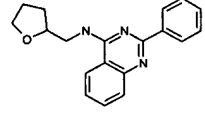
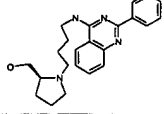
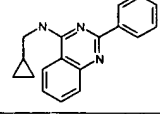
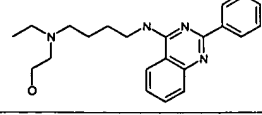
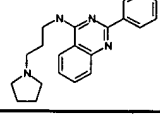
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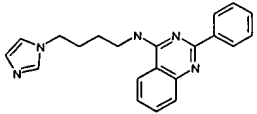
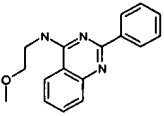
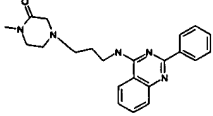
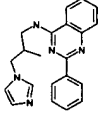
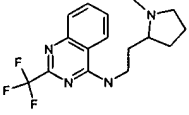
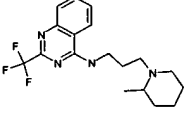
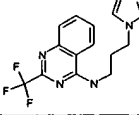
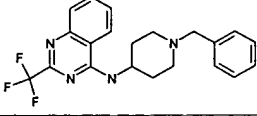
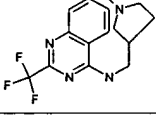
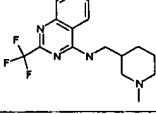
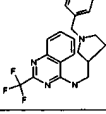
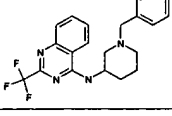
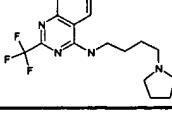


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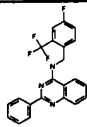
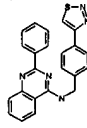
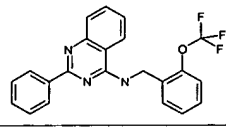
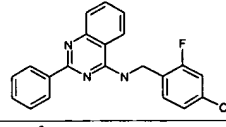
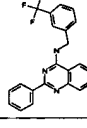
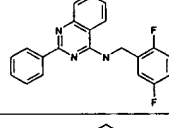
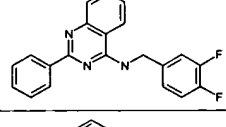
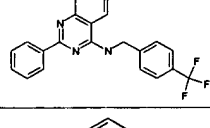
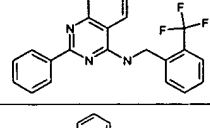
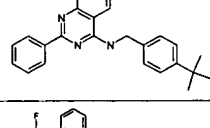
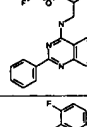
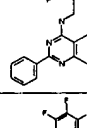
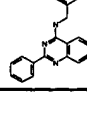
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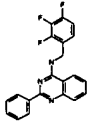
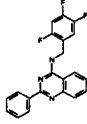
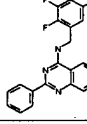
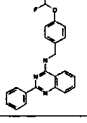
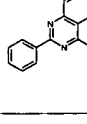
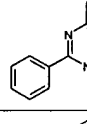
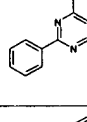
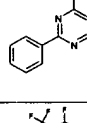
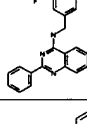
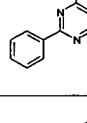
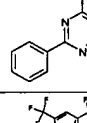
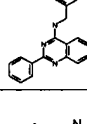
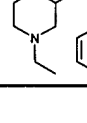
				
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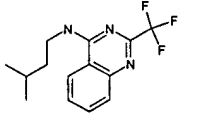
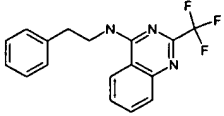
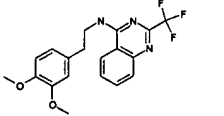
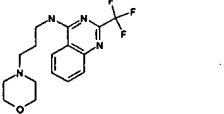
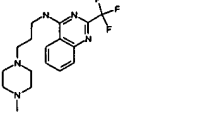
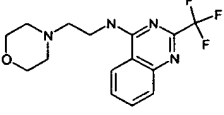
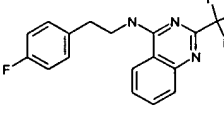
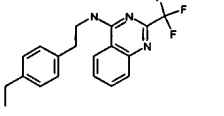
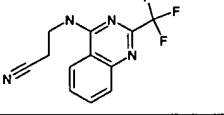
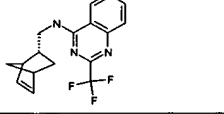
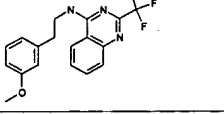
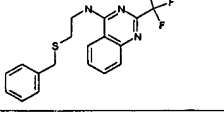
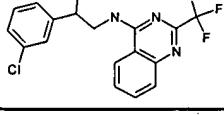
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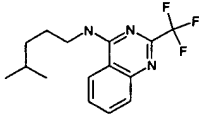
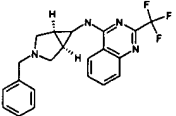
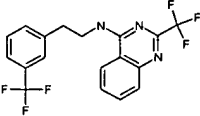
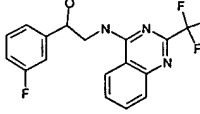
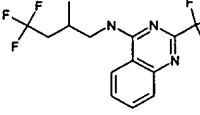
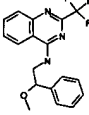
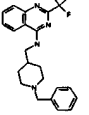
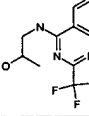
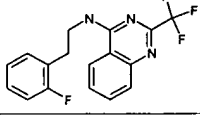
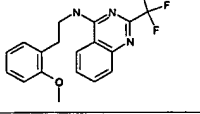
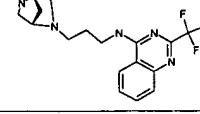
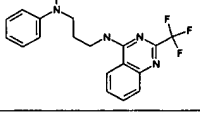
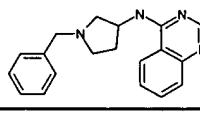
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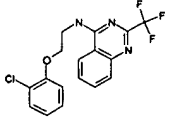
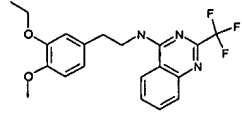
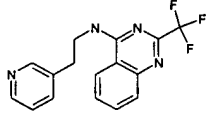
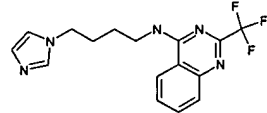
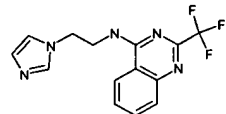
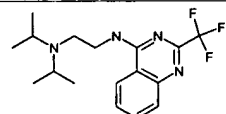
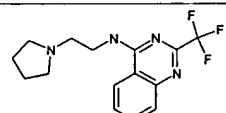
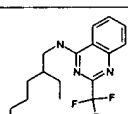
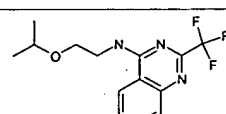
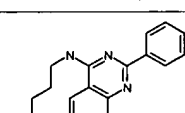
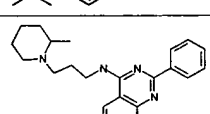
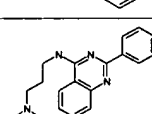
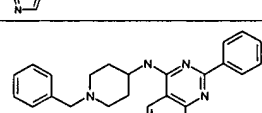
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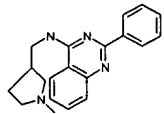
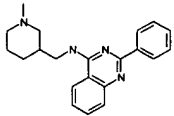
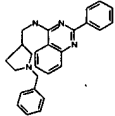
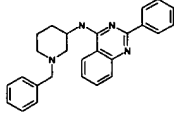
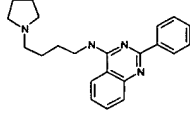
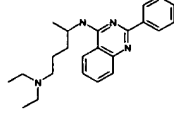
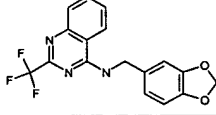
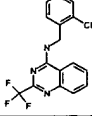
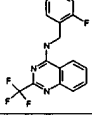
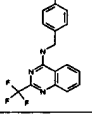
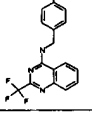
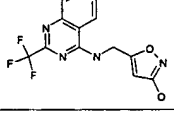
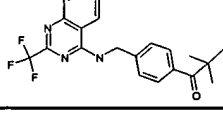
				
				
				
				
				
				
				
				
				
				
				
				
				

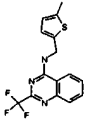
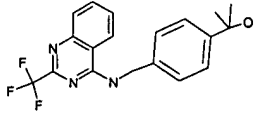
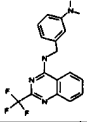
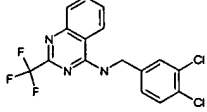
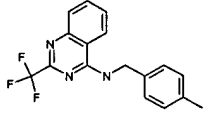
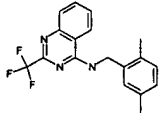
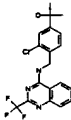
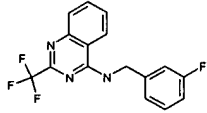
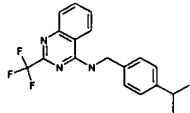
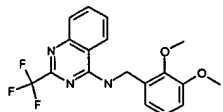
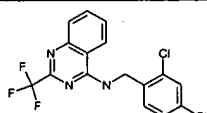
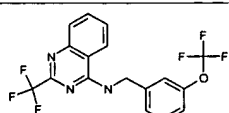
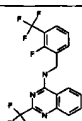
				
				
				
				
				
				
				
				
				
				
				
				
				

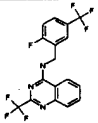
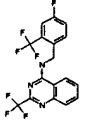
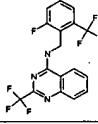
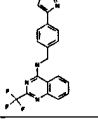
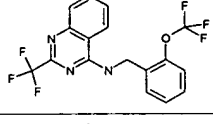
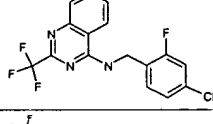
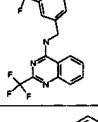
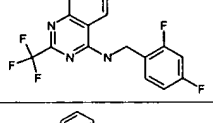
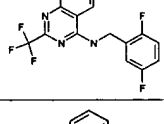
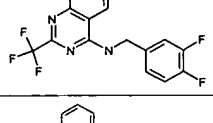
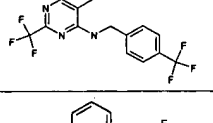
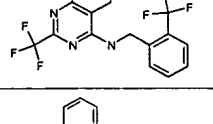
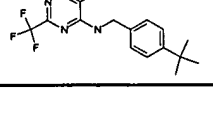
				
				
				
				
				
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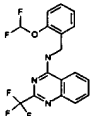
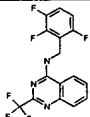
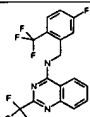
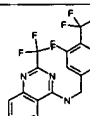
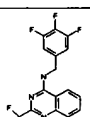
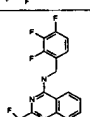
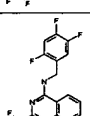
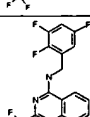
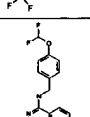
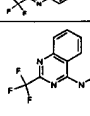
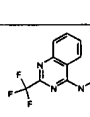
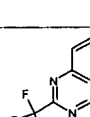
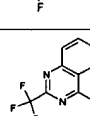
				
				
				
				
				
				
				
				
				
				
				
				
				

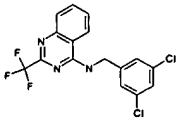
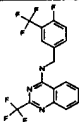
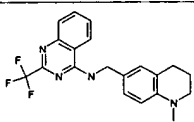
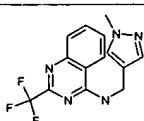
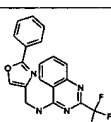
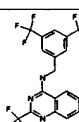
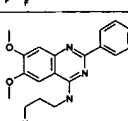
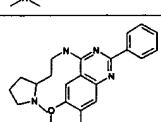
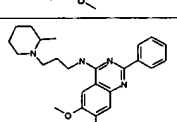
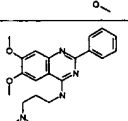
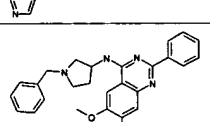
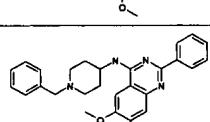
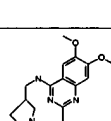
				
				
				
				
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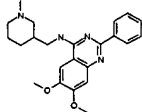
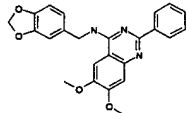
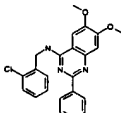
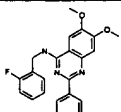
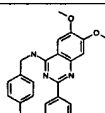
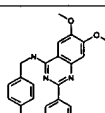
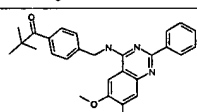
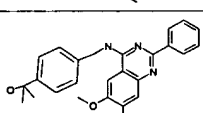
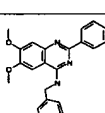
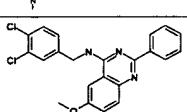
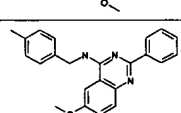
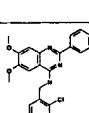
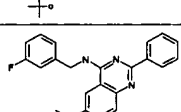
			
			
			
			
			
			
			
			
			
			
			
			
			

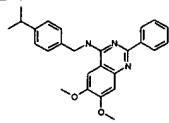
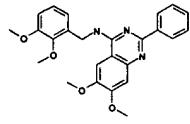
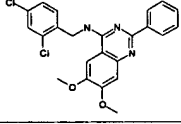
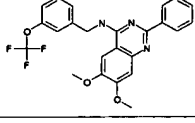
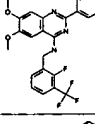
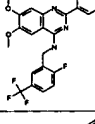
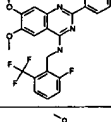
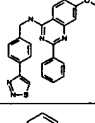
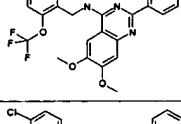
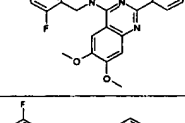
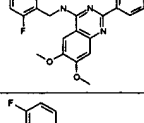
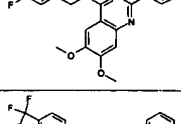
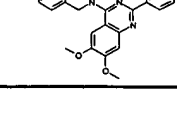
				
				
				
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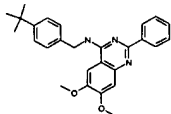
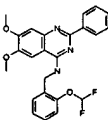
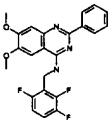
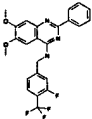
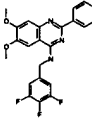
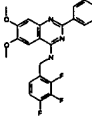
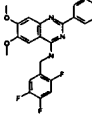
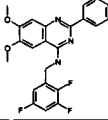
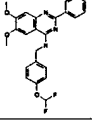
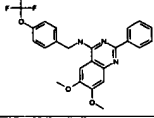
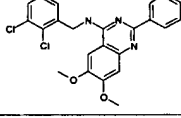
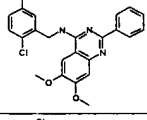
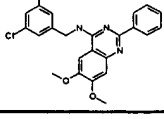
				
				
				
				
				
				
				
				
				
				
				
				
				

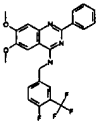
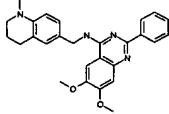
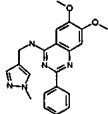
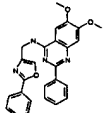
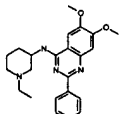
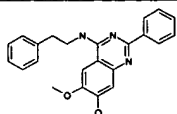
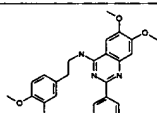
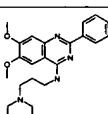
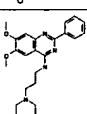
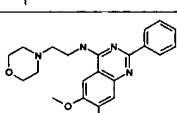
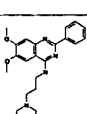
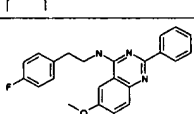
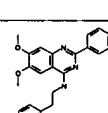
				
				
				
				
				
				
				
				
				
				
				
				
				

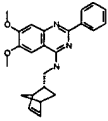
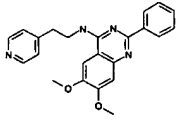
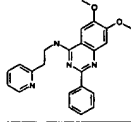
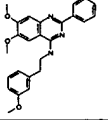
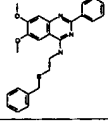
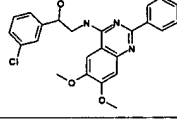
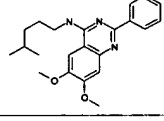
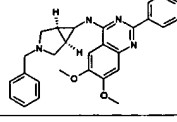
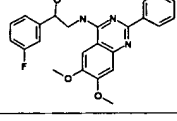
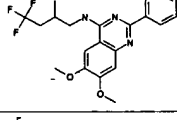
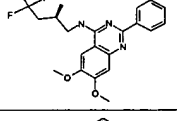
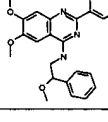
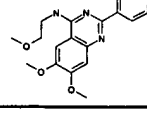
				
				
				
				
				
				
				
				
				
				
				
				
				

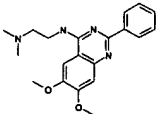
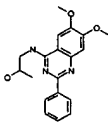
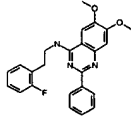
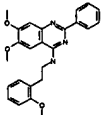
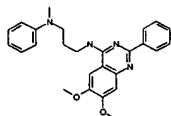
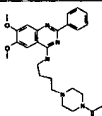
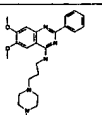
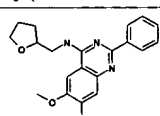
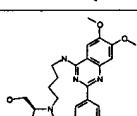
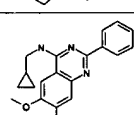
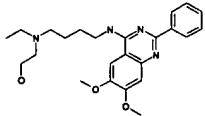
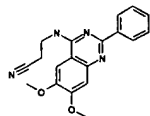
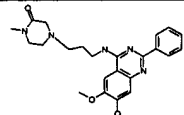
				
				
				
				
				
				
				
				
				
				
				
				
				

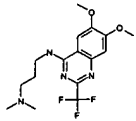
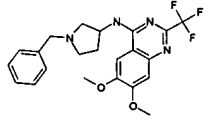
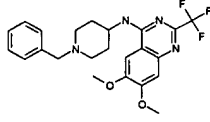
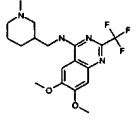
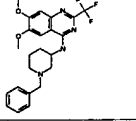
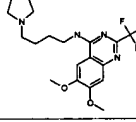
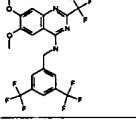
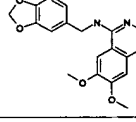
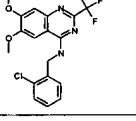
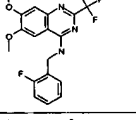
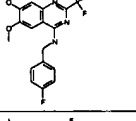
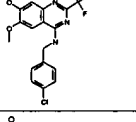
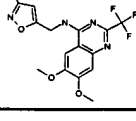
				
				
				
				
				
				
				
				
				
				
				
				
				

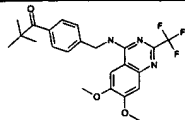
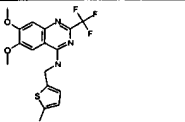
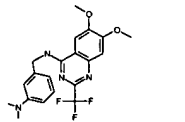
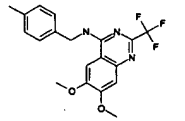
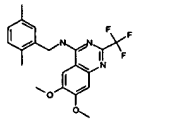
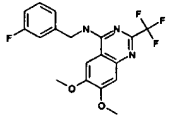
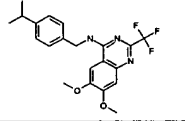
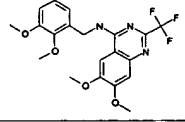
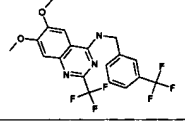
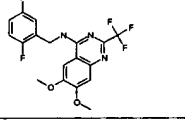
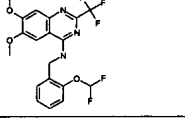
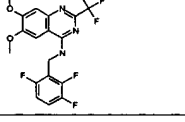
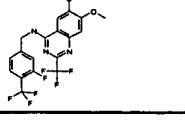
				
				
				
				
				
				
				
				
				
				
				
				
				

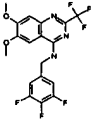
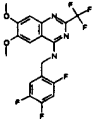
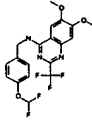
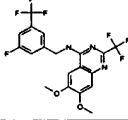
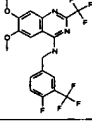
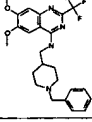
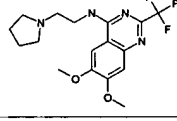
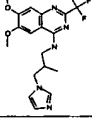
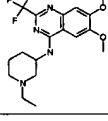
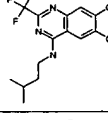
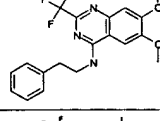
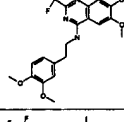
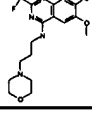
				
				
				
				
				
				
				
				
				
				
				
				
				

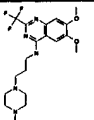
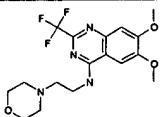
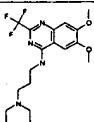
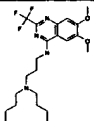
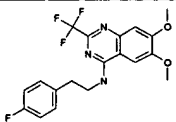
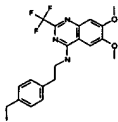
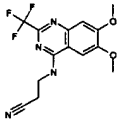
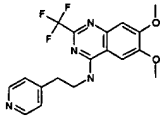
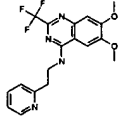
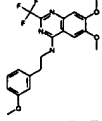
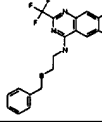
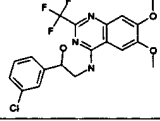
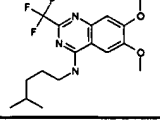
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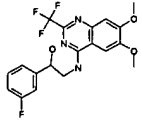
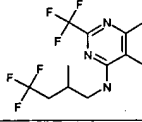
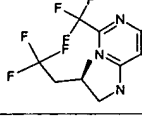
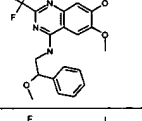
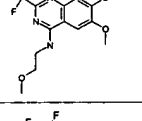
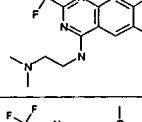
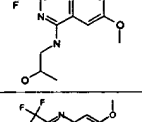
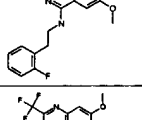
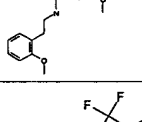
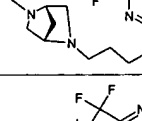
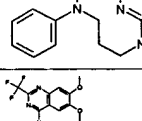
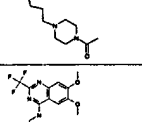
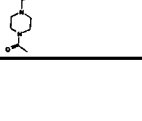
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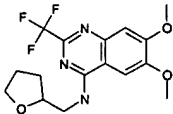
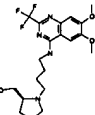
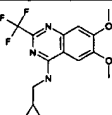
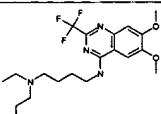
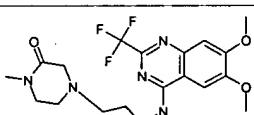
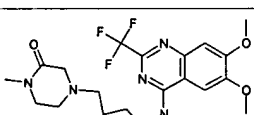
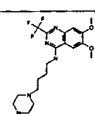
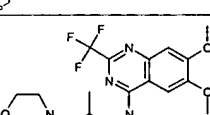
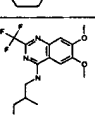
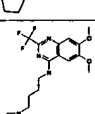
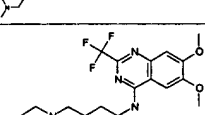
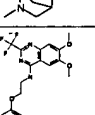
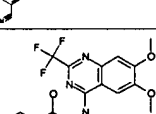
				
				
				
				
				
				
				
				
				
				
				
				
				

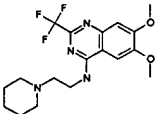
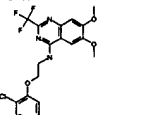
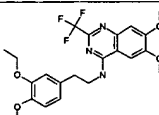
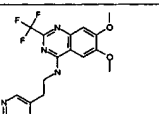
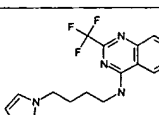
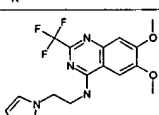
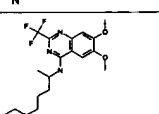
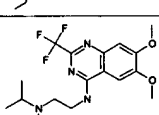
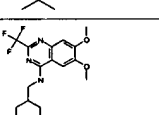
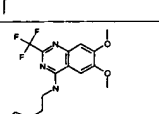
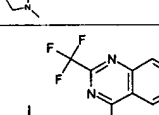
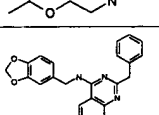
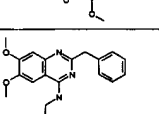
			
			
			
			
			
			
			
			
			
			
			
			
			

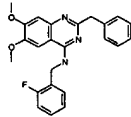
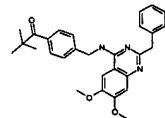
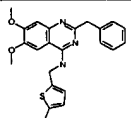
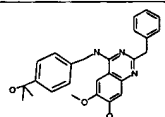
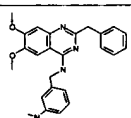
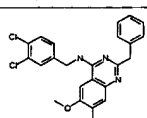
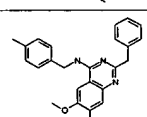
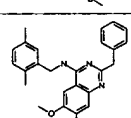
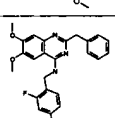
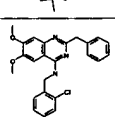
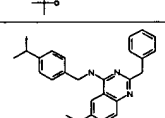
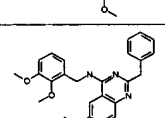
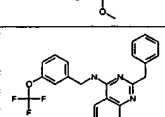
			
			
			
			
			
			
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